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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,366	03/31/1998	GUDMUNDUR JOHANNSSON	0151/00211	6749

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/050,366	JOHANNSSON ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24, 41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/23/02 has been entered.

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, DECLARATION AND STATUS OF THE CLAIMS

2. The amendment, remarks and declaration under 37 C. F.R. 1.132 filed 9/23/02 are acknowledged, entered and considered. In view of Applicant's request claim 42 and a new abstract have been added. Thus, claims 22-24 and 41-42 are now pending in the application. The objections to the abstract is withdrawn in view of Applicant's submission of new abstract. However, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained.

DECLARATION UNDER 37 C.F.R. 1.132: INSUFFICIENT

3. The declaration under 37 CFR 1.132 filed 9/23/02 is insufficient to overcome the rejection of claims 22-24, 41 and newly submitted claim 42 based upon Johansson et al. (Metabolism, Vol. 44, No. 9, pp. 1126-1129, September 1995) applied under 35 U.S.C. 103(a) as

set forth in the last Office action because the declaration fails to set forth factual scientific data supporting the statements made in the declaration. There is no evidence in the instant specification to support and /or demonstrate Dr. Werner's opinion which states that a therapeutic response to growth hormone administration in a growth hormone deficient patient cannot be used to predict a response to growth hormone administration in a patient who is not growth hormone deficient. Specifically, the effect of growth hormone administration on insulin resistance in a growth hormone deficient patient cannot be used to predict an effect of growth hormone administration on insulin resistance in a patient who is not growth hormone deficient. There is no disclosure in the instant specification nor the claims are directed to administration of growth hormone on insulin resistance in a growth hormone deficient patient, rather, the specification and the claims are directed to administering growth hormone to a patient having metabolite syndrome comprising primary insulin resistance and abdominal/visceral obesity in an amount effective for decreasing insulin resistance of said patient. Thus, there is no factual support in a form of evidence or data to substantiate the opinion, and as such, the declaration is inadequate to overcome the rejection based on the prior art of record because there is/are no factual evidence supporting the statement; See *In re Carroll,* 601 F.2d 1184, 202 USPQ 571 (CCPA 1979).

With respect to paragraph 5 of the declaration which asserts that the reference of Johansson et al. Does not teach or suggest insulin resistance in individuals with metabolic syndrome and thus, cannot be used to suggest growth hormone administration to decrease insulin

resistance in individual having metabolic syndrome, thus, the reference does not provide an enabling disclosure of the present invention, and therefore does not support a rejection of the claims under 35 U.S.C. 103(a) is unpersuasive because the declaration presented asserts that the reference relied upon is inoperative, the claims represented by Applicant must be distinguished from the alleged inoperative reference disclosure; See *In re Crosby,* 157 F.2d 198, USPQ 73 (CCPA 1946); also, *In re Epstein*, 32 F.3d 1559, 31 USPQ2d 1817 (Fed. Cir. 1994). Thus, the declaration under 37 C.F.R. 1.132 is insufficient because it refer(s) only to the system described in the above referenced application and not to the claims of the application. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716. Therefore, in view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

4. It is noted that a proper *prima facie* case of obviousness is overcome by evidence that the prior art teaches away from the invention, or by evidence that the claimed invention yields unexpected superior results. Since there is/are no amendment to the claims and Applicant has not presented rebuttal evidence in order to prevail the *prima facie* obviousness presented by the Examiner. Hence, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained for the same reasons discussed on the previous Office action as reiterated below:

CLAIM REJECTIONS-35 U.S.C. § 103(a)

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

It is noted that the rejection under 35 U.S.C. 102(b) has been withdrawn in favor to the rejection under 35 U.S.C. 103(a). This is not a new rejection since Applicant has received the 103 rejection in combination with 102(b) rejection in the previous Office actions including the Office action mailed 6/19/01 (Paper No. 25). This does not preclude the Examiner from making this Office action Final and the Examiner will respond to Applicant's arguments as they apply to the rejection set forth.

6. Claims 22-24, 41 and newly joined claim 42 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. (Metabolism, Vol. 44, No. 9, pp. 1126-1129, September 1995)

Johansson teaches that "Growth Hormone-Deficient Adults Are Insulin-Resistant". Abstract including the Title. This reference further teaches the use of rhGH "after 6 months of rhGH treatment, insulin sensitivity was restored to baseline values. It is likely that the favorable changes in the body composition, such as an increase in lean body mass and a decrease in abdominal and visceral adipose tissue, induced by rhGH treatment the insulin antagonistic effect of GH", page 1129. See, the entire document.

An ordinary art skilled at the time the invention was made would have immediately envisaged the use of GH for treating insulin resistance in a patient having the (Metabolic Syndrome comprising) abdominal/visceral obesity in view of the teachings of the art, absent evidence to the contrary.

ARGUMENTS ARE NOT PERSUASIVE

7. The rejection of claims 22-24, 41 and newly joined claim 42 under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. (Metabolism, Vol. 44, No. 9, pp. 1126-1129, September 1995)

Applicant's arguments filed 1/23/02 and 9/23/02 and a declaration under 37 C.F.R. 1.132 therewith have been fully considered but they are not persuasive. With respect to the declaration, See the discussion above on paragraph 3.

Applicant has argued that the reference of Johansson et al. does not teach or suggest a method for treating insulin resistance in a patient with Metabolic Syndrome by decreasing insulin resistance, rather, the reference teaches that growth hormone deficient patients are insulin resistant, while the present invention teaches the use of growth hormones to decrease insulin resistance associated with Metabolic Syndrome. Further, Applicant argues that after 26 weeks of growth hormone treatment insulin sensitivity returns to base line value, while the present invention teaches that after 9 months of treatment with growth hormone in Metabolic Syndrome individuals there is a decrease in insulin resistance is not persuasive. Contrary to Applicant's arguments, the prior art clearly teaches as disclosed on page 1129 that the use of growth hormone would result in favorable changes in body compositions, such as an increase in lean body mass and a decrease in abdominal and visceral adipose tissue which is induced by rhGH treatment the insulin antagonist effect of GH.

With respect to Applicant's argument that after 26 weeks of growth hormone treatment insulin sensitivity returns to base line value, while the present invention teaches that after 9 months of treatment with growth hormone in Metabolic Syndrome individuals there is a decrease in insulin resistance is noted. However, this argument is irrelevant because the claims are not directed to duration of growth hormone treatment in Metabolic Syndrome individuals to decrease

in insulin resistance (i.e., 6 months treatment versus 9 months treatment) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ 2d 1057 (Fed. Cir. 1993). Thus, Applicant's argument is not commensurate to the scope of the claims. Should the claims be amended, the reference Johansson et al. on page 1128, right column bridging page 1129 stated that in a previous study, we showed that rhGH treatment induced a markedly worsened insulin resistance after 6 weeks, due to a decrease in the effect of insulin on glucose utilization. However, after 6 months of rhGH treatment, insulin sensitivity was restored to baseline values. Hence, showing a transient phenomenon wherein insulin sensitivity can deteriorate during rhGH treatment. Furthermore, the reference suggests that hypothetically, a further improvement in insulin sensitivity is possible, since exercise capacity and physical activity continue to improve beyond the first 6 months of rhGH treatment. Thus, in view of the above, it would be conventional and within the ordinary skill in the art to which this invention pertains to select the appropriate optimum duration time of growth hormone treatment for the intended purpose to decrease insulin resistance in Metabolic Syndrome individuals. Therefore, the instant invention's duration time of growth hormone treatment, which fall within the scope of the prior art duration time of growth hormone treatment would have been *prima facie* obvious from said prior art disclosure to a person of ordinary skill in the art at the time the invention was made because in the absence of sufficient objective factual evidence or unexpected results to the contrary, Applicant's claims if amended to such, would be directed to optimization

of an "art recognized variable" which is well within the purview of one of ordinary skill in the art, *In re Boesch*, 617 F. 2d. 272, 205 USPQ 215 (CCPA 1980). With respect to Applicant's allegation that the reference of Johansson et al. does not provide an enabling disclosure of the present invention, and therefore does not support a rejection of the claims under 35 U.S.C. § 103(a) has been considered but is not persuasive. The reference is published prior art and the reference has not been demonstrated as inoperable.

ACTION IS FINAL, FIRST ACTION FOLLOWING REQUEST FOR CONTINUED EXAMINATION UNDER 37 CFR. 1.114

8. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDENCE

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

AAM/Mohamed/AAM

November 21, 2002

christopher S.F. Low

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